



Government of **Western Australia**  
Department of **Health**

# Preimplantation Genetic Diagnosis (PGD) in Western Australia





Human 'somatic' cells have 46 chromosomes each, made up of the 23 chromosomes provided by the egg and the sperm cell from each parent. Each chromosome has coded information organised into 'genes' which are made of DNA.

Serious genetic conditions can arise when errors in this information occur. This includes when errors within a gene are passed from parent to child, or when an embryo develops abnormally with more or fewer than the correct number (46) of chromosomes.

People with a high risk of having a child born with a serious genetic condition may seek to test for the condition before the child is born. This may be possible, either:

- **during** a pregnancy – by tests following amniocentesis or chorionic villus sampling. This is known as prenatal diagnosis
- or
- **before** a pregnancy – by testing an embryo created through in vitro fertilisation (IVF). This is known as **Preimplantation Genetic Testing**.

For many people at risk of passing on a serious genetic condition to their children, genetic testing *before* the implantation of an embryo may be preferable to prenatal diagnosis during pregnancy. This may be because of the emotional impact of terminating a pregnancy where the fetus has been found to carry a serious genetic condition. There are also health risks associated with miscarriage and termination. For some people, termination may also pose ethical concerns.



## What is Preimplantation Genetic Testing?

Every cell in an embryo, including the cells that will go on to develop into the placenta, has the same genetic make up. In Preimplantation Genetic Testing, one or more cells are removed, or biopsied, from an embryo and either their chromosomes or DNA are tested for the presence of a genetic abnormality.

Preimplantation Genetic Testing of embryos is generally divided into:

- **Preimplantation Genetic Diagnosis (PGD)**

One or more cells from an embryo are tested for the presence of a gene or genes that may harm the embryo and developing child. PGD also includes looking at chromosomes that may be of the correct number, but where a piece (or more) of chromosome is translocated onto another chromosome.

and

- **Preimplantation Genetic Screening (PGS)**

One or more cells from an embryo are tested for the number of chromosomes in the embryo. This is also known as aneuploidy screening; aneuploidy is when a cell shows an abnormal number of chromosomes.



This brochure will look at the steps involved in PGD in Western Australia. Further information on prenatal diagnosis and PGS is available in other Department of Health brochures.

## **What can Preimplantation Genetic Diagnosis test for?**

PGD can detect many genetic conditions, including many single gene conditions and translocations.

### ***Single gene conditions***

Some conditions are due to a single genetic alteration. If the exact gene has not been identified or there is no test for the gene, PGD is not possible. However, hundreds of genes have been identified, and PGD is available to test for many of these single gene conditions. These include Huntington's disease, thalassaemia, sickle cell anaemia and cystic fibrosis.

### ***Sex linked conditions***

Some genetic conditions such as Duchenne muscular dystrophy and haemophilia only affect males. Unaffected female embryos or male embryos can be chosen to avoid the specific genetic condition. Choosing the sex of an embryo is only permitted to avoid passing on serious disease.

### ***Translocations***

Translocations are chromosomal abnormalities where part of one chromosome has been transferred to another chromosome. The extent to which this affects a person may vary, depending on what translocation is present. A person with a translocation in his or her genetic makeup may not wish to risk conceiving a child who may carry a harmful translocation. If a woman has suffered many miscarriages, it may be recommended that she and her partner undergo genetic testing to look for a translocation.

## Preimplantation Genetic Diagnosis and the Reproductive Technology Council

In Western Australia, approval from the WA Reproductive Technology Council (Council) is required before a fertility clinic can create embryos for PGD. This is to make sure that testing on embryos is only carried out when there is a high risk of a serious genetic condition (not for other reasons such as sex selection of embryos which is not permitted in Australia) and to make sure that patients have received genetic counselling appropriate for their situation.

When making a decision about PGD, the Council considers the risk and severity of the condition, how safe and reliable the test is, and the impact of the condition on both a prospective child and the family.

## How do we seek approval for Preimplantation Genetic Diagnosis?

The steps described below may take several months to complete:

- 1) Discussion** with a genetic counsellor and clinical geneticist at Genetic Services of WA. This may follow a GP, specialist or self-referral. This consultation will cover a wide range of issues, including the experience and understanding that the couple have of the condition, the risk of passing the condition onto a child, the impact of the condition on a child and the family, and reproductive options for the couple, including PGD.
- 2) Consultation with a fertility clinic**  
Your genetic counsellor can inform you about clinics offering PGD services. You can choose which clinic you would like to attend, though not all fertility



clinics will offer PGD services. You will need a GP or specialist referral for you to undertake IVF.

### **3) Fertility clinic appointment/counselling**

At your first clinic appointment you should receive information about the IVF process, the risks, how embryos will be tested for the genetic condition and the costs associated with each step of the process. The clinic will also provide access to an approved counsellor – one counselling session will be included in the cost of each IVF cycle. The role of counselling is to ensure that you are aware of the physical and emotional impact of IVF treatment and to discuss ways to manage this.

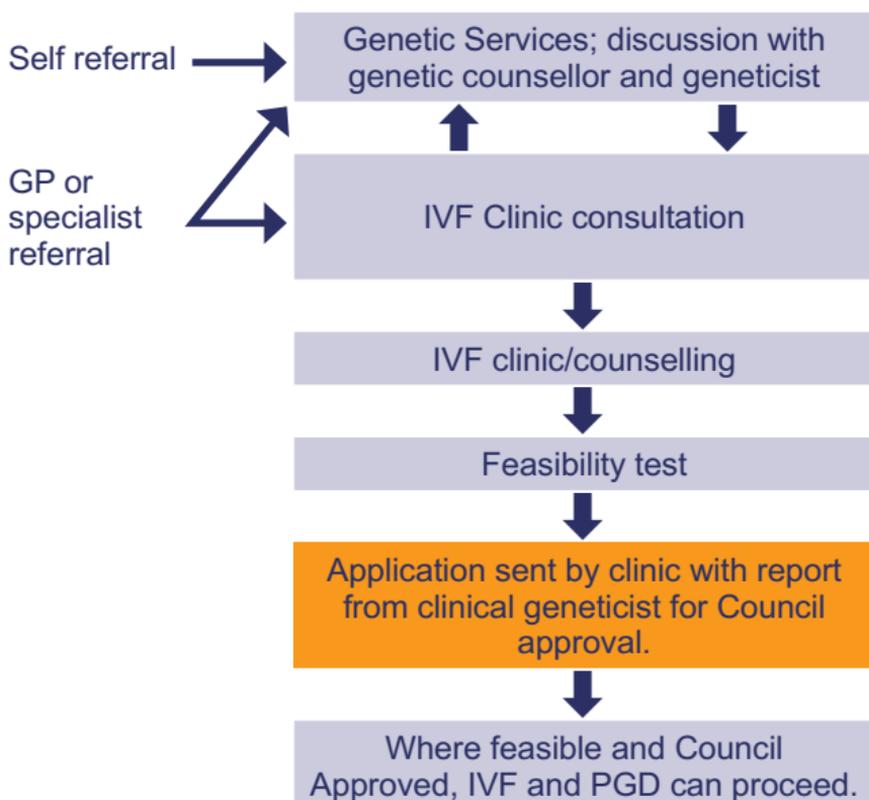
### **4) A feasibility test**

This complex laboratory test is to find out if it will be possible to test embryos for the genetic condition in question. In most cases a new test will have to be developed specifically. You and your partner will have to provide a small sample of blood for this test and other family members may also be asked to provide a blood sample. If the test is not feasible, PGD cannot be done. The feasibility test may take some time – 3 to 6 months, depending on the genetic condition it is testing for.

### **5) Application to the Reproductive Technology Council for approval**

For single gene disorders and translocations, the fertility clinic will apply to the Council on your behalf to undertake PGD. The approval process usually takes a month but can take longer for more complex applications. A report from the clinical geneticist will need to accompany an application sent to the Council to undertake PGD.

## Steps involved in the Preimplantation Genetic Diagnosis process



## What does an in vitro fertilisation cycle with Preimplantation Genetic Diagnosis involve?

PGD can only test embryos when they have been created by IVF or intracytoplasmic sperm injection (ICSI). IVF is a laboratory procedure where an egg is fertilised through natural sperm penetration, but outside of a woman's body. ICSI is a similar procedure, but differs from routine IVF in that a single chosen sperm is inserted into the egg for fertilisation. ICSI is the preferred method for the creation of embryos for PGD.



An IVF cycle for PGD will be coordinated by the medical and laboratory teams at a fertility clinic, and can proceed after the fertility clinic receives Council approval to undertake PGD for a couple.

The main steps in an IVF/PGD cycle include:

### **1) Fertility drugs are administered to a woman**

These may be given orally, or by injection over a 2 to 4 week period. The fertility drugs act to stimulate more than one ovarian follicle to mature and provide a number of eggs for fertilisation.

### **2) Blood and ultrasound tests**

These are used to check the woman's follicle development so that egg collection can be timed. These tests are also to avoid overstimulating the ovaries.

### **3) Egg collection**

The woman is placed under a light anaesthetic or sedation (and occasionally a general anaesthetic) so that eggs may be collected with the help of a vaginal ultrasound probe. This will be performed by a gynaecologist.

### **4) Fertilisation**

After egg collection, the eggs will be fertilised with sperm in the laboratory through IVF or ICSI. Sperm may have been freshly collected or previously collected and frozen. The fertilised eggs are matured or 'cultured' until 3 or 5 days of age.

### **5) Biopsy (removal of cells for testing)**

Cell removal is carried out on embryos:

- at 3 days of age when an embryo will usually have between 6 to 8 cells,  
or
- at 5 days of age when an embryo, known as a blastocyst, will have around 100 cells.

A laser is used to open the outside shell of the embryo, and the cell/s are carefully separated from the remaining embryonic cells. In most cases, the 'hole' or deficit will close over, and the embryo will develop as it should. However, a very small percentage of embryos will not continue to develop following embryo biopsy.

## **6) Laboratory analysis**

The biopsied cells are then prepared and sent to a laboratory to be tested for the specific gene or translocation. Testing of the cells may be carried out interstate – this will depend on the clinic providing the IVF and PGD and the type of testing required. Polymerase chain reaction (PCR) is the most common laboratory method used for PGD.

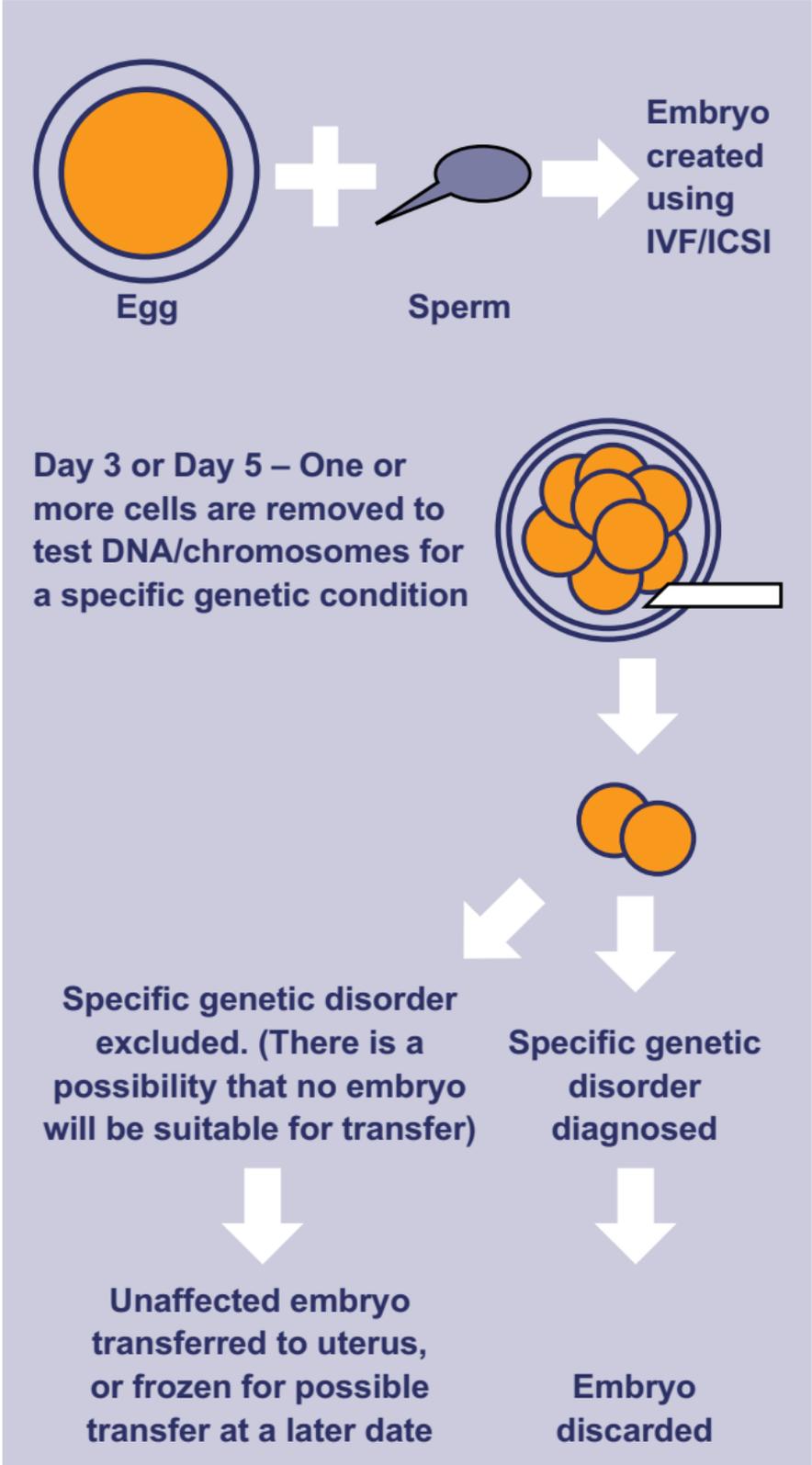
## **7) Freezing of embryos**

When embryos are tested on day 3, it may be possible to transfer the embryos after biopsy/PGD as the PGD results are usually back within 2 days. When day 5 (blastocyst) embryos are tested, they will require freezing following the biopsy in order to await results.

## **8) Transfer**

If the PGD results show that an embryo is suitable for transfer, the embryo (usually one) is transferred using a catheter that has been guided into the woman's uterus. Any remaining embryos that are suitable for transfer can be frozen and stored for later use. Unfortunately, there is always a chance that no embryos created from an IVF cycle will be suitable for transfer.

# In vitro fertilisation and biopsy of embryos for Preimplantation Genetic Diagnosis



## Accuracy of Preimplantation Genetic Diagnosis

PGD has an accuracy of around 98%, so the chance of a false result is very low. However, as every couple has some risk of having a child with a genetic condition and PGD is a highly specific test for only one condition, prenatal testing will be recommended if a pregnancy is achieved. It is recommended that prenatal testing options for other common genetic conditions be discussed with a fertility specialist, obstetrician or genetic counsellor.

## What risks are involved?

The process of IVF and PGD poses some risks to the woman and the embryo. These may include:

- Health risks of the IVF cycle
- An embryo may not develop after fertilisation of an egg
- Not all embryos will be suitable for biopsy
- The embryo may not develop after biopsy
- There may not be any unaffected embryos available for transfer
- Test results may be inconclusive
- Results are not 100% accurate
- No pregnancy is achieved, even after the transfer of an unaffected embryo.



## Is there a risk to the child from In vitro fertilisation or Preimplantation Genetic Diagnosis?

Long term studies have shown that there is some increased chance of birth defects in children born from assisted reproductive technologies (ART) compared to naturally conceived children.<sup>1</sup> In WA, the birth defect rate for the last 20 years for *all* births (both natural and ART) has been approximately 5-7%.<sup>2</sup> From these figures, the overall risk for birth defects for ART births will be approximately 6-10%. The reason for the increased risk is not yet known, but it is not generally considered a reason to not use ART such as IVF and ICSI. However, these risks should be discussed with your fertility clinic or genetic counsellor. Results from the use of PGD both internationally and in Australia have so far shown that PGD poses no *additional* risk to children created through IVF, and of course PGD aims to avoid a known genetic condition being passed on to a child.

## What are the likely costs?

IVF for PGD involves a number of medical and laboratory services, so out of pocket expenses can be high. While there are Medicare and private health insurance rebates for IVF, there are currently no rebates for the PGD procedure.

The first IVF/PGD cycle will be the most costly as it will include the feasibility test plus the collection of eggs and creation of embryos. Further IVF/PGD cycles should not require a feasibility test. In addition, an IVF/PGD cycle may produce more than one suitable embryo. These tested embryos may be frozen and stored, to allow their transfer in the future.

An estimation of current costs can be noted here by your fertility clinic, or Genetic Services of WA.

	Estimated cost
Laboratory work up for feasibility	
IVF/ ICSI treatment	
PGD analysis	
<b>Total:</b>	
Frozen embryo transfer (of previously tested embryo)	



Fertility clinics offering PGD can provide an up to date schedule of fees that includes the out of pocket expenses associated with IVF and PGD. An idea of current costs can also be accessed from the Council website [www.rtc.org.au](http://www.rtc.org.au) under Consumer Information. Please note these estimated costs will vary between fertility clinics.

### **What are the success rates?**

A summary of results collected from Australian and New Zealand fertility clinics<sup>3</sup> showed that in 2007, the live delivery rate per IVF/ PGD cycle was approximately 18%, which means one child was born for every five to six IVF/PGD cycles undertaken.

As with IVF, a number of IVF/PGD cycles may be needed to achieve the birth of a child, with the possibility that a pregnancy may still not be achieved even after an unaffected embryo has been transferred. Your genetic counsellor or fertility clinic will be able to discuss these matters with you further.



## Is Preimplantation Genetic Diagnosis the right choice for you?

If you are concerned about having a child with a harmful genetic condition, a genetic counsellor can discuss whether PGD is a suitable choice for you. Matters that should be discussed include the risks and implications of having an affected child, PGD and IVF, and prenatal screening and diagnosis. As outlined in this brochure, a decision to have PGD is also a decision to have IVF, rather than to conceive naturally. As with any assisted reproductive technology, unfortunately there is no guarantee of a successful outcome. However, PGD may offer couples who have a significant risk of passing on a serious genetic condition to their children a means of conceiving a child free of that genetic condition.

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- <sup>1</sup> Hansen M, Bower C, Milne E, de Klerk N, Kurinczuk JJ. Assisted reproductive technologies and the risk of birth defects – a systematic review. *Hum Reprod* 2005 Feb; 20 (2) :328-338
  - <sup>2</sup> Bower C, Rudy E, Callaghan A, Quick J, Cosgrove P, Nassar N. Report of the Birth Defects Registry of Western Australia 1980 – 2008. King Edward Memorial Hospital, No.16; 2009. p6
  - <sup>3</sup> Wang YA, Chambers GM, Dieng M, Sullivan EA . Assisted reproductive technology in Australia and New Zealand 2007. Canberra. AIHW. Assisted reproduction technology series no. 13. Cat. no. PER 47. 2009



Reproductive Technology Council

**For more information please contact:**

Genetic Services Western Australia  
Kind Edward Memorial Hospital  
374 Bagot Road  
Subiaco WA 6008  
Phone: (08) 9340 1525

A list of clinics currently offering PGD and PGS services is available on the Reproductive Technology Council website [www.rtc.org.au](http://www.rtc.org.au) under Consumer Information.

This document can be made available in alternative formats such as computer disc, audio tape or Braille, on request.